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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/997,628	11/15/2001	David Botstein	P2730P1C30	7410

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EXAMINER	
WEGERT, SANDRA L	
ART UNIT	**PAPER NUMBER**
1647	

SHORTENED STATUTORY PERIOD OF RESPONSE	MAIL DATE	DELIVERY MODE
3 MONTHS	03/30/2007	PAPER

Please find below and/or attached an Office communication concerning this application or proceeding.

If NO period for reply is specified above, the maximum statutory period will apply and will expire 6 MONTHS from the mailing date of this communication.

Office Action Summary	Application No.	Applicant(s)	
	09/997,628	BOTSTEIN ET AL.	
	Examiner	Art Unit	
	Sandra Wegert	1647	

-- The MAILING DATE of this communication appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) OR THIRTY (30) DAYS, WHICHEVER IS LONGER, FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133). Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *10 January 2007*.

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *119-123* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *119-123* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☒ The drawing(s) filed on *15 November 2001* is/are: a)☒ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

Replacement drawing sheet(s) including the correction is required if the drawing(s) is objected to. See 37 CFR 1.121(d).

11)☐ The oath or declaration is objected to by the Examiner. Note the attached Office Action or form PTO-152.

Priority under 35 U.S.C. § 119

12)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____.

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO/SB/08) Paper No(s)/Mail Date _____.
4) ☐ Interview Summary (PTO-413) Paper No(s)/Mail Date. _____.
5) ☐ Notice of Informal Patent Application
6) ☐ Other: _____.

DETAILED ACTION

Status of Application, Amendments and/or Claims

The Remarks submitted 10 January 2007 have been considered. Claims 119-123 are under consideration in the instant application.

Claim Rejections - 35 USC § 101 and 35 USC § 112

The following is a quotation of 35 U.S.C. 101:

> **Whoever invents or discovers any new and useful process, machine, manufacture, or composition of matter, or any new and useful improvement thereof, may obtain a patent therefor, subject to the conditions and requirements of this title.**

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> **The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.**

Claims 119-123 are rejected under 35 U.S.C. 101 because the claimed invention is not supported by either a specific and substantial asserted utility or a well-established utility. Novel biological molecules lack well-established utility and must undergo extensive experimentation. The basis for this rejection is set forth for claims 119-123 in the previous Office Action (11 October 2006).

Claims 119-123 are directed to an antibody that specifically binds to the polypeptide of SEQ ID NO: 349. The claims also recite that the antibody is monoclonal or humanized. The claims recite that the antibody is an antibody fragment or that the antibody is labeled.

Applicants' arguments in the response submitted 10 January 2007, as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons:

To summarize, for utility of the claimed PRO1097 antibodies, Applicants rely on the gene amplification data for the gene encoding the polypeptide. Applicants argue that Example 143 of the specification discloses that the PRO1097 gene is significantly overexpressed in colon and lung tumors as compared to normal control. Applicant asserts that the PRO1097 polypeptide is useful as a diagnostic marker and a therapeutic target for treatment for tumors. Briefly, it is the examiner's position that the present specification fails to disclose the physiological significance of the PRO1097 polypeptide or what the correlation between PRO1097 DNA, PRO1097 mRNA and PRO1097 polypeptide expression is or the significance of any such correlation in colon and lung tumors. A specific benefit does not exist in currently available form because the skilled artisan would not know if the expression of the PRO1097 polypeptide would be upregulated, down-regulated, or unchanged in cancer. Until some actual and specific significance can be attributed to the protein identified in the specification as PRO1097, the instant claimed invention is incomplete. Therefore, Applicants' assertion of the overexpression of the PRO1097 gene does not impute a specific and substantial utility to the PRO1097 polypeptide or claimed antibodies.

Specific arguments are addressed below.

At pp. 3-4 of the Response, Applicants assert that it was well known in the art at the time the invention was made that gene amplification is an essential mechanism for oncogene activation. Applicants state that Example 143 of the specification discloses that the inventors

isolated genomic DNA from a variety of primary cancers and cancer cell lines that are listed in Table 8. They go on to explain that a ΔCt value of at least 1.2 was observed for PRO1097 in at least two of the tumors listed in Table 8. Applicants argue that PRO1097 showed approximately 1.2 ΔCt units which corresponds to $2^{1.21}$-$2^{1.23}$ fold amplification or 2.313 fold or 2.346 fold amplification in lung tumors as an example. Applicant submits that the specification has not only disclosed that the DNA copy number for the gene encoding PRO1097 is increased in two different tumors, but has also quantified the degree of gene amplification observed in each of these tumors. Applicants also cite the Declaration of Dr. Audrey Goddard to contend that absence any evidence to the contrary, the 2.313 fold or 2.346-fold amplification disclosed for the PRO1097 gene is significant. Applicants state that a positive result from one or a few tumors, where the nucleic acid was amplified, but not from other tumors, indicates that the nucleic acid can be used as a marker for diagnosing the presence of that kind of tumor in which it was amplified.

Applicants' arguments have been fully considered but are not found to be persuasive. In the instant case, the specification provides data showing a very small increase in DNA copy number in two different types of tumor tissue (lung and colon). However, there is no evidence regarding whether or not PRO1097 mRNA or polypeptide levels are also increased in these cancers. Further research needs to be done to determine whether the small increase in PRO1097 DNA supports a role for the peptide in the cancerous tissue; such a role has not been suggested by the instant disclosure. It is not known whether PRO1097 is expressed in corresponding normal tissues, and what the relative levels of expression are. Therefore, it is not clear that the reported amplification is significant. In the absence of any of the above information, all that the

specification does is present evidence that the DNA encoding PRO1097 is amplified in a variety of samples and invites the artisan to determine the significance of this increase. One cannot determine from the data in the specification whether the observed "amplification" of nucleic acid is due to increase in chromosomal copy number, or alternatively due to an increase in transcription rates. It remains that, as evidenced by Pennica et al., the issue is simply not predictable, and the specification presents a mere invitation to experiment. This further experimentation is part of the act of invention and until it has been undertaken, Applicants' claimed invention is incomplete (see *Brenner v. Manson*, (1966, 383 U.S. 519, 148 USPQ 689)).

In regards to the Declaration under 37 C.F.R. §1.132 by Dr. Goddard (Remarks, p. 5), the examiner maintains that the Declaration is not pertinent, as it is drawn to the significance of the amplification of the nucleic acids, and fails to address the issue of the claimed antibodies, which bind to the protein encoded by the nucleic acid which is alleged to be significantly amplified in cancer. Applicants discuss the accuracy of the Taq DNA polymerase assay, stating that the Taqman PCR technique is sensitive enough to detect at least a 2-fold increase in gene copy number and that this increase is significant and useful. Applicants direct the Examiner to the portion of Goddard declaration that describes the gene amplification technique in the present application and to the references that attest to the use of this technique in diagnostic and prognostic fashion. This argument has been fully considered but is not deemed persuasive because it evinces that the instant specification provides a mere invitation to experiment, and not a readily available utility. The PRO1097 gene has *not* been associated with tumor formation or the development of cancer, nor has it been shown to be predictive of such. The specification merely demonstrates that the PRO1097 nucleic acid was amplified in two types of cancer

samples (lung and colon), to a minor degree (about 2.3). No mutation or translocation of PRO1097 has been associated with any type of cancer versus normal tissue.

Furthermore, the Declaration does not provide data such that the examiner can independently draw conclusions. Only Dr. Goddard's conclusions are provided in the Declaration. It is noted that the literature cautions researchers from drawing conclusions based on small changes in transcript expression levels between normal and cancerous tissue. For example, Hu et al. (of record) analyzed 2286 genes that showed a greater than l-fold difference in mean expression level between breast cancer samples and normal samples in a microarray (p. 408, middle of right column) and discovered that, for genes displaying a 5-fold change or less in tumors compared to normal, there was no evidence of a correlation between altered gene expression and a known role in the disease. However, among genes with a 10-fold or more change in expression level, there was a strong and significant correlation between expression level and a published role in the disease (see discussion section).

Therefore, the Goddard declaration is not persuasive as it relates only to the issue of nucleic acids and not to the instantly-claimed subject matter, which is antibodies. Furthermore because of the issues described above, even *if* the claims were directed to nucleic acids, the arguments presented by Dr. Goddard would still not have been persuasive.

At the bottom of p. 5 through p. 6 of the Response, Applicant asserts that the negative control taught in the specification was known in the art at the time of filing, and accepted as a true negative control as demonstrated by use in peer reviewed publications, including Pennica et al. Applicant points out that Pennica explains the WISP copy number in each colon tumor DNA was compared with pooled normal DNA from 10 donors. Applicant contends that Pennica et al.

use the same control for their gene amplification experiments as that described in the instant specification. Applicants submit that Pitti et al. (submitted with the Response of 22 August 2005) describe the analysis of DNA copy number in genomic DNA from primary tumors relative to pooled genomic DNA from peripheral blood leukocytes. Applicant argues that Bieche et al. (submitted with the Response of 22 August 2005) used normal leukocyte DNA derived from a small subset of breast cancer patients and note that the results of the study are consistent with those reported in the literature. Applicants conclude from these studies that the art demonstrates that pooled normal blood samples are considered to be a valid negative control for gene amplification experiments.

Applicants' arguments have been fully considered but are not found to be persuasive. Specifically, although Pennica et al. and Pitti et al. compare gene amplification of specific genes in colon and lung tumors to pooled DNA from 10 healthy normal donors, Pennica et al. and Pitti et al. are not attempting to utilize the data generated from the experiments for diagnostic purposes (as is Example 143 of the instant application). Secondly, Bieche et al. is simply utilizing real-time PCR to validate an assay for the detection and determination of the copy numbers of the three most frequently amplified genes in breast tumors (*myc, ccnd1*, and *erbB2*). That research group compared the results for 108 breast tumors with previous Southern-blot data for the same samples (abstract; p. 662, column 1). The genes studied by Bieche et al. were already well-known in the art to be amplified in breast cancer. Thus, in that case it was not necessary to utilize matched normal tissue samples.

Regarding the instant application, the specification provides data purportedly showing a slight increase in DNA copy number in two different types of tumor tissue (lung and colon) of

PRO1097. However, PRO1097 is novel and has not been characterized in the pre- or post-filing date art. It is not known whether PRO1097 is expressed in corresponding normal tissues, and what the relative levels of expression are. There is no structure/function analysis in the specification regarding the putative protein encoded by the PRO1097 gene. It is not disclosed, and based upon the sequence searches in this case, the Examiner cannot find any reason to suspect, that the protein encoded by the PRO1097 gene would confer any selective advantage on a cell expressing it. It has no known homology to any protein that would be expected to *confer a selective advantage* to a tumor cell. Additionally, gene amplification does not reliably correlate with polypeptide over-expression, and thus the level of polypeptide expression must be tested empirically. The instant specification does not provide this additional information; thus the skilled artisan would need to perform additional experiments.

At p. 6 through p. 7 of the Response, Applicants contend that it is known in the art that detection of gene amplification can be used for cancer diagnosis regardless of whether the increase in gene copy number results from intrachromosomal changes or from chromosomal aneuploidy. Applicant states that amplification of a gene, whether by aneuploidy or any other mechanism, is useful as a diagnostic marker.

Applicants' arguments have been fully considered but are not found to be persuasive. Aneuploidy is a feature of damaged tissue, and is commonly found in lung tissues, which are subject to constant environmental damage. It does not invariably or inevitably lead to cancer. Rather, such damaged cells are generally removed by the body. The development of cancer is the exception, as evidenced by the fact that the general population is constantly suffering damage to lung cells via air pollution, whereas lung cancer remains relatively rare. The specification of the

instant application asserts that since the nucleic acid encoding PRO1097 is slightly overexpressed in colon and lung tumor samples, the PRO1097 polypeptide may be used in the diagnostic determination of the presence of cancers. However, a positive result can also correlate with *damaged*, but not cancerous, lung and colon epithelium. Merely because aneuploidy may be an initial step in the *formation of cancer* does not equate with a substantial assertion of a diagnostic tool *for cancer* for the encoded PRO1097 protein.

At p. 7 and p. 15-16 of the 10 January 2007 Response, Applicants assert that the evidentiary standard to be used throughout *ex parte* examination in setting forth a rejection is a preponderance of the totality of the evidence under consideration. Applicants further argue that the references cited by the Examiner (Pennica et al, Chen et al., Haynes et al., Hu et al., etc.) do not suffice to make a *prima facie* case that there is not a "more likely than not" generalized correlation between increased mRNA expression and increased polypeptide levels. Applicants state that the references cited by the examiner are either irrelevant, not contrary to Applicants' arguments, or actually offer support for Applicants' positions. They further contend that they have submitted enough rebuttal evidence such that it is more likely than not that a person of skill in the art would be convinced, to a reasonable probability, that the asserted utility is true.

Applicants' arguments have been fully considered but are not found to be persuasive. The previous rejections set forth that the assertion of utility is not substantial. In the previous Office Action of 10 January 2007, the Examiner made a *prima facie* showing that the claimed invention lacks utility and also provided a sufficient evidentiary basis for factual assumptions relied upon in establishing the *prima facie* showing (Pennica et al., Sen et al., Chen et al., Haynes

et al., Hu et al.). These references, taken into consideration with the disclosure, indicate to the skilled artisan that it is more likely than not that PRO1097 polypeptide and antibodies are not useful as cancer diagnostic agents. Essentially, Applicants have not provided evidence to demonstrate that gene amplification correlates with polypeptide over-expression or that the PRO1097 polypeptide of the instant application is supported by a specific and asserted utility or a well established utility, such that it would be useful to detect it with the claimed antibody. The Examiner has fully considered all evidence of record and has responded to each substantive element of Applicants' response. It is noted to Applicant that MPEP § 2107.02 (part VI) also states that "only where the totality of the record continues to show that the asserted utility is not specific, substantial, and credible should a rejection based on lack of utility be maintained".

It is also noted that the specification of the instant application does not teach a change in DNA, mRNA, or protein level of PRO1097. The specification simply discloses a measurement of PRO1097 DNA in colon and lung tumor samples as compared to a blood control. There are no teachings in the specification as to the differential expression of PRO1097 DNA, mRNA, or protein in the progression of colon or lung cancers or in response to different treatments of hormones (for example). Therefore, the Examiner maintains that Applicants' measurement of a slight increase of PRO1097 DNA does not provide a specific and substantial utility for the encoded protein and claimed antibody.

At p. 7 of the Response, Applicants contend that a review of the correlation coefficient data presented in the Chen et al. paper indicates that it is more likely than not increased mRNA expression correlates with increased protein expression.

Applicants' arguments have been fully considered but are not found to be persuasive. Chen et al. compared mRNA and polypeptide expression for a cohort of genes in the same lung adenocarcinomas. Only 17% of 165 polypeptide spots or 21% of the genes demonstrated a significant correlation between polypeptide and mRNA expression levels. Chen et al. clearly state that "the use of mRNA expression patterns by themselves, however, is insufficient for understanding the expression of protein products" (p. 304) and "it is not possible to predict overall protein expression levels based on average mRNA abundance in lung cancer samples" (pp. 311-312). The instant specification does not provide additional information regarding whether or not PRO1097 mRNA or polypeptide is overexpressed in colon or lung tumors; thus the skilled artisan would need to perform additional experiments to reasonably confirm such. Since the asserted utility for the PRO1097 polypeptides and claimed antibodies is not in currently available form, the asserted utility is not substantial.

Applicants argue at p. 8 of the Response that Gygi et al. indicate a general trend of correlation between protein [expression] and transcript levels. Applicants conclude that the Gygi data meets the "more likely than not standard" and shows that a positive correlation exists between mRNA and protein.

Applicants' arguments have been fully considered but are not found to be persuasive. While Gygi et al. does not address whether changes in mRNA levels will be reflected as observable changes in protein levels, the reference nonetheless demonstrates that observed mRNA levels do not necessarily correspond to observed protein levels. Gygi et al. state: "the correlation between mRNA and protein levels was insufficient to predict protein expression

levels from quantitative mRNA data. Indeed, for some genes, while the mRNA levels were of the same value the protein levels varied by more than 20-fold. Conversely, invariant steady-state levels of certain proteins were observed with respective mRNA transcript levels that varied by as much as 30-fold. Our results clearly delineate the technical boundaries of current approaches for quantitative analysis of protein expression and reveal that simple deduction from mRNA transcript analysis is insufficient" (abstract; p. 1727, top of col 2; p. 1730, concluding sentence).

Similarly, at p. 14-15 of the Response, Applicants assert that Futcher et al. (1999) conducted a study of mRNA and protein expression in yeast and reported a good correlation among protein abundance, mRNA abundance, and codon bias. Applicants' arguments have been fully considered but are not found to be persuasive. Futcher et al concludes that "[t]his validates the use of mRNA abundance as a rough predictor of protein abundance, at least for relatively abundant proteins [emphasis added]" (p. 7368, col 1). Futcher et al. also admits that Gygi et al. performed a similar study and generated similar data, but reached a different conclusion. Futcher et al. conclude that "Gygi et al. feel that mRNA abundance is a poor predictor of protein abundance" (p. 7367, col 1, 1st full paragraph).

At p. 3 of the 10 January 2007 Response, Applicants assert that the Patent Office has failed to meet its initial burden of proof that Applicants' claims of utility are not substantial or credible. Applicants contend that the Examiner's reasoning is based on a misrepresentation of the scientific data presented in the above cited references and application of an improper, heightened legal standard.

Applicants' arguments have been fully considered but are not found to be persuasive. The truth, or credibility, of the assertion of utility has not been questioned. Rather, the Rejection sets forth that the assertion of utility is not substantial. The preponderance of evidence supports this position. See Pennica et al., Chen et al. (who found only 17% of 165 polypeptide spots or 21% of the genes had a significant correlation between polypeptide and mRNA expression levels in lung adenocarcinoma samples), Hu et al. (who reviewed 2286 genes reported in the literature to be associated with breast cancer) and Haynes et al. These references, taken into consideration with the disclosure, indicate to the skilled artisan that it is more likely than not that the PRO1097 polypeptide and antibodies are not useful as cancer diagnostic agents.

At p. 4 of the 10 January 2007 Response, Applicants argue that Orntoft et al., teach that, in general, gene amplification correlates with increased mRNA expression.

Applicants' arguments have been fully considered but are not found to be persuasive. Specifically, the issue in the instant application is whether or not gene amplification is predictive of increased mRNA levels and, in turn, increased protein levels. There is no demonstration of *any* mRNA level for PRO1097, either in the specification or in *any* of the numerous declarations that have been submitted; hence the theoretical correlation of mRNA with protein is not probative. Furthermore, there is strong opposing evidence showing that gene amplification is not predictive of increased mRNA levels in normal and cancerous tissues and, in turn, that increased mRNA levels are frequently not predictive of increased polypeptide levels. See, e.g., Pennica et al., Hu et al., and Haynes et al. In fact, the methodology used in the Orntoft reference is different from that of Applicant. What is significant remains that the levels of amplification observed by Applicants are consistent with aneuploidy, and that such amplification is not accepted in the art

as being predictive of increased protein expression, which increased expression would be essential for the claimed antibodies to have the asserted utility. It must be emphasized that arguments of counsel alone cannot take the place of evidence in the record once an examiner has advanced a reasonable basis for questioning the disclosure. See *In re Budnick*, 537 F.2d at 538, 190 USPQ at 424; *In re Schulze*, 346 F.2d 600, 145 USPQ 716 (CCPA 1965); *In re Cole*, 326 F.2d 769, 140 USPQ 230 (CCPA 1964). Orntoft et al. only compared genes from non-invasive transitional cell carcinomas to genes from invasive transitional cell carcinomas. There was no comparison between genes in cancerous versus non-cancerous tissue.

An additional reference that provides evidence that gene amplification does not predictably or even predominantly lead to increased transcription is Li et al., (Oncogene, 2006, Vol. 25, p. 2628-2635). Li et al. used a functional approach that integrated simultaneous genomic and transcript microarray, proteomics, and tissue microarray analyses to directly identify putative oncogenes in lung adenocarcinoma. On p. 2633, right column, Li et al. state: "*In our study, 68.8% of the genes showing over-representation in the genome did not show elevated transcript levels*, implying that at least some of these genes are 'passenger' genes that are concurrently amplified because of their location with respect to amplicons but *lack biological relevance in terms of the development of lung adenocarcinoma.*"

In conclusion, in the instant case, the asserted utility that PRO1097 polypeptides and claimed antibodies are useful as diagnostic markers for cancer is not substantial in that further research is required to reasonably confirm a real world context of use. In order for PRO1097 polypeptide and antibodies to be useful as cancer diagnostics, there must be a detectable change

in the amount or form of PRO1097 polypeptide between cancerous and healthy tissue. In the instant case, the evidence of record indicates that (1) gene amplification does not reliably correlate with increased mRNA levels and (2) increased mRNA levels do not reliably correlate with increased polypeptide levels in healthy tissue or cancerous tissue (see Pennica et al., Haynes et al., Hu et al., etc). In light of these arguments, the skilled artisan would have viewed the gene amplification results as preliminary with respect to the utility of the encoded polypeptides, and would have had to experiment further to reasonably confirm whether or not the PRO1097 polypeptides and claimed antibodies can be used as cancer diagnostic agents.

35 U.S.C. § 112, first paragraph (Enablement)

Claims 119-123 are also rejected under 35 U.S.C. 112, first paragraph. Specifically, since the claimed invention is not supported by either a specific and substantial asserted utility or a well established utility for the reasons set forth above, one skilled in the art clearly would not know how to use the claimed invention. The basis for this rejection is set forth at p. 18-19 of the previous Office Action (11 October 2006).

Applicants' arguments (10 January 2007) as they pertain to the rejections have been fully considered but are not deemed to be persuasive for the following reasons.

Applicants state that a credible, substantial, and asserted utility has been disclosed above for the PRO1097 polypeptide and claimed antibodies. Applicants' arguments have been fully considered but are not found to be persuasive. Specifically, since Applicant has not provided evidence to demonstrate that the PRO1097 polypeptide has a specific and substantial asserted utility or a well-established utility, one skilled in the art would not know how to use the claimed

invention. It is noted that the instant specification is required to teach one skilled in the art how to make and use the PRO1097 polypeptide and antibodies.

The rejections of claims 119-123 under 35 U.S.C. § 101 and § 112, first paragraph (utility, enablement) have been made and maintained in the previous three Office Actions. Essentially, Applicants assert that the PRO1097 antibody is useful as a diagnostic marker for colon and lung tumors. It is the Examiner's position that the present specification fails to disclose the physiological significance of the PRO1097 polypeptide, or its cognate antibody, or what the correlation is among PRO1097 DNA, PRO1097 mRNA and PRO1097 polypeptide expression or the significance of any such correlation in colon and lung tumors. The state of the art has been cited and found to support the examiner's positions. It is the examiner's opinion that the issue has been fully developed and, given the mixed teachings of the art, the examiner maintains that gene amplification of PRO1097 is not predictive of any correlation between the polypeptide (which would be detected by the claimed antibody) and any cancer.

Conclusion

No claim is allowable.

All claims are drawn to the same invention claimed in the application prior to the entry of the submission under 37 CFR 1.114 and could have been finally rejected on the grounds and art of record in the next Office action if they had been entered in the application prior to entry under 37 CFR 1.114. Accordingly, **THIS ACTION IS MADE FINAL** even though it is a first action

after the filing of a request for continued examination and the submission under 37 CFR 1.114. See MPEP § 706.07(b). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event, however, will the statutory period for reply expire later than SIX MONTHS from the mailing date of this final action.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Sandra Wegert whose telephone number is (571) 272-0895. The examiner can normally be reached Monday - Friday from 9:00 AM to 5:00 PM (Eastern Time). If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Brenda Brumback, can be reached at (571) 272-0961.

The fax number for the organization where this application or proceeding is assigned is 571-273-8300.

Information regarding the status of an application may be obtained from the Patent Application Information Retrieval (PAIR) system. Status information for published applications

may be obtained from either Private PAIR or Public PAIR. Status information for unpublished applications is available through Private PAIR only. For more information about the PAIR system, see http://pair-direct.uspto.gov. Should you have questions on access to the Private PAIR system, contact the Electronic Business Center (EBC) at 866-217-9197 (toll-free).

SLW
22 March 2007

Eileen B. O'Hara

EILEEN B. O'HARA
PRIMARY EXAMINER